

Application No.: 10/553,584
Filing Date: October 17, 2005

AMENDMENTS TO THE SPECIFICATION

Kindly amend the header and paragraph [0001] as follows:

RELATED APPLICATIONS CLAIM OF PRIORITY

[0001] The present application is a U.S. national phase application under 35 U.S.C. § 371(c) of international application no. PCT/US2004/011900, and claims the benefit of priority to U.S. provisional application 60/463,047, filed April 16, 2003, both of which application is are incorporated herein by reference in their entirety.

Kindly amend paragraph [0008] as follows:

[0008] The first and second electrochemical signals may be substantially free of an electrochemical signal from intercalated probe molecule. The probe molecule may be substantially free of polynucleotides having a length of at least 4 based bases, e.g., 8 bases.

Kindly amend paragraph [0010] as follows:

[0010] In some embodiments, the probe molecule may comprise at least two cyclic groups. The probe molecule may include at least three 6-membered rings. The probe molecule may be an anthracycline, methylene blue, or derivative thereof, e.g., the probe molecule may be is selected from the group consisting of daunomycin, doxorubicin, methylene blue, toluidine blue O, azure A, azure B, azure C, thionin, and derivatives thereof.

Kindly amend paragraph [0101] as follows:

[0101] In certain embodiments, working electrode 214 is associated with a plurality of probe molecules having an electrochemical activity that depends upon the presence or absence of a target compound. For example, the target compound may modify the electrochemical activity of the probe molecule by modifying the number of probe molecules in electrochemical communication with the electrode. Alternatively or in combination, the target compound may modify an electrochemical characteristic of the probe molecule itself. For example, interaction between the probe molecule and the target compound may modify an oxidation or reduction potential of an electrochemically active moiety of the probe molecule. To determine the presence of the target compound, the working electrode is used to obtain one or more electrochemical

signals from the probe molecules. The electrochemical signal(s) are used to determine the presence or absence of the target compound.

Kindly amend paragraph [0133] as follows:

[0133] If layer 244 and substrate 242 are formed of different materials, layer 244 may act as a catalyst that modifies a potential at which the probe molecule is oxidized or reduced as compared to a potential at which the probe molecule ~~60~~ 232 would be oxidized or reduced at surface 248 of substrate 242. For example, layer 244 may reduce an absolute magnitude of an oxidation or reduction potential of the probe molecule.

Kindly amend paragraph [0147] as follows:

[0147] Referring to FIGS. 7a-7e, a plurality of target compounds are detected electrochemically using probe molecules 1160 and 1162, which respectively comprise a first portion 1164, 1166 and a second portion 1168, 1170. First portions 1164, 1166 may be identical to one another and may include any of the probe molecules discussed herein. Second portion 1168 of probe molecule 1160 preferentially associates with a first probe target molecule, e.g., polynucleotide 1161, as opposed to a second, different probe target molecule, e.g., polynucleotide 1163. Second portion 1170 of probe molecule 1162 preferentially associates with second polynucleotide 1163 as opposed to first polynucleotide 1161.

Kindly amend paragraph [0173] as follows:

[0173] A user may introduce to the electrochemical detection chamber a preferably liquid sample in which the amount of a target polynucleotide is to be determined. Preferably, target polynucleotide, if present in the liquid, is hybridized with a second polynucleotide sufficiently complementary to the target polynucleotide to hybridize therewith. If the target polynucleotide and a second, complementary polynucleotide are in single stranded form, the liquid may be subjected to an annealing step, such as by cooling the liquid, to allow hybridization of the target polynucleotide and second complementary polynucleotide.

Kindly amend paragraph [0201] as follows:

[0201] Referring to FIG. 11a 11b, a first electrochemical signal 204 and a second electrochemical signal 206 are plotted as a function of potential applied to the first, heated portion of the sample. Referring to FIG. 11b 11a, a first electrochemical signal 200 and a second electrochemical signal 202 are plotted as a function of potential applied to the second portion of sample, which had not been subjected to heating at 115° C. A maximum current 201 of the first signal 200 is substantially less greater than a maximum current 203 of the second signal 202. The reduction in current is indicative of a reduced amount DOX associated with the working electrode when the second signal 202 was obtained. The amount of DOX associated with the electrode decreases because some DOX dissociates from the working electrode and associates with double-stranded amplicons present in the detection region 312. In contrast, first and second electrochemical signals 204, 206 of the first, heated portion of the sample are not different because of the lack of amplification caused by thermal deactivation of the taqman enzyme. The absence of amplicons in the heated portion of sample and the presence of amplicons in second portion of sample was confirmed via gel electrophoresis.

Kindly amend paragraph [0211] as follows:

[0211] Repeated electrochemical signals were obtained from a probe molecule without substantial oxidization or reduction thereof. A microfluidic device having a DOX associated electrode was prepared as discussed above. Electrochemical signals were obtained by scanning the electrical potential applied to the electrode without applying a potential sufficient to oxidize or reduce the DOX. The most negative potential was -550 mV. The area under the electrochemical signal response was less than the full response if the scan included potentials of between -550 and -1000 mV. A plurality of measurements of the amount of probe molecule reversibly immobilized with respect to an electrode surface may be performed without electrode regeneration.